as Attachment 3 is the compare copy of the claims, marked to show all of the changes relative to the previous version of the claims.

REMARKS

Claims 1-39 are currently pending in the application. Claim 1 has been amended to incorporate the limitation of claim 2, and claim 16 has been amended to incorporate the limitation of claim 17. Claims 2 and 17 have been cancelled herein without prejudice or disclaimer of the subject matter claimed therein. Claims 3, 6, 18, and 21 have been amended to correct the claim dependencies. Claims 6, 19, 20, and 21 have been amended herein to correct obvious typographical errors and to better define the claimed invention. Accordingly, no new matter is introduced by these amendments. Accordingly, after entry of these amendments, claims 1, 3-16, and 18-39 will be pending in the application.

The specification has been amended to correct obvious typographical errors. Accordingly, no new matter has been introduced by way of these amendments, and entry of these amendments is respectfully requested.

The outstanding rejections are addressed individually below.

1. Claims 2-7, 10, 11, 17-22, 25, 26, 32, 33, 35, and 36 are definite.

Claims 2-7, 10, 11, 17-22, 25, 26, 32, 33, 35, and 36 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicant respectfully traverses this rejection.

Claims 2 and 17 stand rejected because the language "at least two 3' terminal ribonucleotides, at least two 5' terminal ribonucleotides, or at least two 3'-terminal and at least two 5' terminal ribonucleotides" is allegedly vague and unclear. Claims 2 and 17 have been cancelled herein; however, this language has been incorporated into independent claims 1 and 16. Applicant respectfully submits that this language is clear. This language is clearly providing three alternatives: 1) the oligonucleotide has at least

two 3′ terminal ribonucleotides; 2) the oligonucleotide has at least two 5′ terminal ribonucleotides; and 3) the oligonucleotide has at least two 3′ terminal ribonucleotides and at least two 5′ terminal ribonucleotides. Table 2 clearly depicts such alternatives, where the location of the ribonucleotides of the oligonucleotide are underscored.

Accordingly, as Applicant submits that this language is definite, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claims 6 and 21 stand rejected because the language "consist essentially of four 3′-terminal ribonucleotides and four 3′-terminal ribonucleotides, flanking 13 deoxynucleotides" is allegedly vague and unclear. Applicant has amended this language, *inter alia*, to correct a typographical error in order to indicate that the synthetic oligonucleotide comprises four 3′ terminal ribonucleotides and four 5′ terminal ribonculetides, flanking 13 deoxynucleotides. Applicant submits that this language is clear and definite in light of the amendment.

Applicant respectfully requests that this rejection be reconsidered and withdrawn.

2. ***Claims 16-30 and 34-38 are enabled.***

Claims 16-30 and 34-38 stand rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Applicant respectfully traverses this rejection.

Claim 16 has been amended herein to incorporate the limitation of claim 17. However, Applicant respectfully submits that this amendment is not necessary to overcome the above rejection and has been made merely to facilitate prosecution.

Claim 17 has been cancelled herein; therefore, Applicant respectfully submits that the rejection with regard to claim 17 has been rendered moot.

Applicant notes that the Office Action appears to be confused regarding the specific modifications to the oligonucleotide required by the claims. Appplicant respectfully submits that the independent claims as amended require that the 21 nucleotides are linked via phosphorothioate internucleotide linkages, and have at least two 3′ terminal ribonucleotides, at least two 5′ terminal ribonucleotides, or at least two 3′-terminal and at least two 5′ terminal ribonucleotides; however, they do not require 2′-substituted ribonucleotides.

Although Applicant does not necessarily agree with the characterization of all of the cited references, Applicant provides the following remarks.

M.P.E.P § 2164.01 states that 35 U.S.C. § 112, first paragraph, "has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation." (citation omitted) The same section further states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation."

The specification teaches one of skill in the art to how to make the invention (*see, e.g.*, the specification at page 13, line 26 to page 15, line 30 and Example 1, page 32, line 13 to page 33, line 2).

Furthermore, the specification teaches one of skill in the art how to use the invention (*see, e.g.*, the specification at page 20, line 10 to page 21, line 30 (describing pharmaceutical formulations), page 21, line 32 to page 24, line 8 (describing therapeutically acceptable methods and amounts), page 24, lines 10-20 (describing methods of administration), and page 24, line 22 to page 26, line 24 (describing therapeutic formulations and pharmaceutical compositions)).

Therefore, the specification has fully enabled the invention as claimed because it teaches how to make and use the invention without undue experimentation.

Furthermore, the specification provides examples indicating that the invention works as claimed.

The oligonucleotides of the invention have been tested *in vivo* as well as *in vitro.*

To start with, the oligonucleotides of the invention have been tested *in vitro* in a variety of cell types. The specification indicates that *in vitro* experiments were performed analyzing, *inter alia*, the ability of the oligonucleotides of the invention to inhibit existing infections and to protect against infection in MT-4 cells (page 19, lines 18-25 and FIGS: 1 and 2), the preclinical range of anti-HIV activity of various oligonucleotides of the invention using human peripheral blood mononuclear cells, BaL cells and ADA cells (page 26, line 26 to page 30, line 8), and toxicity in fresh human peripheral blood mononuclear cells (page 30, lines 10-28). Several of these experiments are also detailed in the Examples 7 and 8 (page 42, line 13 to page 47, line 27) showing anti-HIV activity in fresh human peripheral blood lymphocytes and fresh human monocyte-macrophages as well as inhibition of acute infection of MT-4 cells.

Furthermore, in *in vivo* testing, the specification at page 31, line 23 to page 32, line 5, and Example 9 (page 47, line 29 to page 52, line 23) of the instant patent application provide description of experiments to evaluate the presence of oligonucleotides of the invention in tissue after oral administration *in vivo*. Furthermore, the specification at page 30, line 30 to page 31, line 7 indicates the bioavailability of oligonucleotides of the invention in rats and monkeys *in vivo*, and the specification at page 31, lines 9-21 indicates the absorption of oligonucleotides of the invention in both rats and monkeys *in vivo*.

Therefore, the specification provides information indicating that the claimed invention does work *in vivo* in accepted animal models.

More specifically, the specification as amended states at page 30, line 30 to page 31, line 4 that "the bioavailability of Oligo 12 was examined *in vivo* and was found to be intravenously and orally bioavailable to rats and monkeys after a single dose . . . [and] synthetic oligonucleotides systemically administered to pregnant murine females were

found to cross the placenta and be available in the blood of embryos *in utero*." Furthermore, the specification at page 31, lines 14-21 states that an oligonucleotide of the invention "was found to be absorbed through the gatstrointestinal tract and accumulated in various organs and tissues" following intravenous or oral administration.

Thus, oligonucleotides of the invention have been shown to work *in vivo*.

Furthermore, many published articles corroborate that antisense oligonucleotides have been shown to be effective. For example, Galderisi et al. (J. Cell. Physiol. (1999) 181:251-57; attached hereto as Attachment 4), indicates that intravenous administration of phosphorothioate oligodeoxynucleotides showed effective and specific antisense inhibition in animal models, that antisense oligodeoxynucleotides have been shown to be effective in preclinical studies, and that some antisense oligodeoxynucleotides have reached clinical trials. The article also teaches that one drug based on antisense technology is now available in the United States. This article provides examples suggesting that "these compounds may have some therapeutic efficacy," including use as antiviral agents.

In addition, Agrawal states, at page v of Antisense Therapeutics, (Sudhir Agrawal, ed.) 1996, (cited pages of which are attached hereto as Attachment 5), that "[t]he results of preclinical studies using oligodeoxynucleotide phosphorothioates have shown that antisense oligonucleotides have good biological activity, pharmacology, pharmacokinetics, and safety both in vitro and in vivo, and they are currently being evaluated in human clinical trials for the treatment of viral infections and cancers."

Zamecnik (attached hereto as Attachment 6) states at page 6 of Antisense Therapeutics, that the synthetic antisense oligonucleotide technology displays promising results in cell-free systems, tissue cultures, and animal models and is at early trial points in human testing against HIV, leukemia, Herpes virus, and other diseases.

Craig, et al. (Exp. Opin. Ther. Patents (1997) 7:1175-1182; attached hereto as Attachment 7) teaches at page 1177 that once a modification to the oligonucleotide

backbone "is found to confer a favorable characteristic, it can then be used in oligonucleotides having different sequences of nucleosides and, thus, provide utility for the treatment of other diseases" as well as discussing information regarding the patentability of antisense technology.

Applicant respectfully asserts that the Examiner may be confusing the requirements under law for obtaining a patent with the requirements for obtaining government approval for marketing a particular drug for human consumption. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d (BNA) 1436 (Fed. Cir. 1995), citing *Scott v. Finney*, 34 F.3d 1058, 1063, 32 U.S.P.Q.2d (BNA) 115, 120 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) Proceedings"). Determining effective parameters for treating HIV-1 or HIV-2 infection in a mammal by administering to the mammal a synthetic oligonucleotide that is specifically complementary to nucleotides 324 to 345 of a conserved *gag* region of the HIV-1 genome set forth as SEQ ID NO: 5 and consisting of 21 nucleotides linked via phosphorothioate internucleotide linkages wherein the oligonucleotide comprises at least two 3′ terminal ribonucleotides, at least two 5′ terminal ribonucleotides, or at least two 3′-terminal and at least two 5′ terminal ribonucleotides and determining the effective amount required for the treatment would be considered a routine process by skilled artisans, and would not require undue experimentation.

Thus, Applicant respectfully asserts that the Examiner's concerns regarding *in vivo* use are inappropriate.

Accordingly, Applicant respectfully requests that this rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

3. Statutory double patenting rejection of claim 39 has been overcome.

Claim 39 stands rejected under 35 U.S.C. § 101 as being allegedly directed to the same invention as that of claim 1 of commonly assigned U.S. Patent No. 5,591,721. Applicant respectfully traverses this rejection.

M.P.E.P. § 804(II)(A.) states that "'Same invention' means identical subject matter. . . ." (citations omitted) This section further states that

> A reliable test for double patenting under 35 U.S.C. 101 is whether a claim in the application could be literally infringed without literally infringing a corresponding claim in the patent. . . . Is there an embodiment of the invention that falls within the scope of one claim, but not the other? If there is such an embodiment, then identical subject matter is not defined by both claims and statutory double patenting would not exist. For example, the invention defined by a claim reciting a compound having a "halogen" substituent is not identical to or substantively the same as a claim reciting the same compound except having a "chlorine" substituent in place of the halogen because "halogen" is broader than "chlorine." . . . (citations omitted)

Applicant submits that claim 39 of the invention is not the same invention as claim 1 of the '721 patent. These two claims contain different limitations that result in embodiments that fall within the scope of one claim, but not the other.

First, claim 1 of the '721 patent is broader in scope due to the fact that the oligonucleotide is 15-25 nucleotides in length (compared to the 21 nucleotides of the oligonucleotide in claim 39) and has at least two 2'-O-methyl ribonucleotides at each end (compared to the four 3' and four 5' flanking 2'-O-methyl ribonucleotides of claim 39).

Second, claim 1 of the '721 patent is narrower in scope due to the fact that the claim requires that the oligonucletide is present intact in the systemic plasma and in liver tissue at least six hours after oral administration. This requirement is narrower

than claim 39, which merely requires that the oligonucleotide is present in intact form in the systemic plasma following oral administration.

Third, claim 39 of the instant application, which is dependent on claim 7, and thereby indirectly dependent on claims 6 and 1, is narrower in scope due to the fact that the claim requires that the oligonucleotide is specifically complementary to nucleotides 324 to 345 of a conserved *gag* region of the HIV-1 genome set forth as SEQ ID NO:5.

Applicant submits that he, Sudhir Agrawal, is the first and only inventor of the subject matter of the instant application, which is not the same invention as that described in claim 1 of the '721 patent.

Therefore, Applicant submits that claim 39 of the application does not define the same invention as claim 1 of the '721 patent. Accordingly, Applicant respectfully requests that this rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

4. ***Claims 1-15 and 31-36 are not obvious over Agrawal et al. in view of Goodchild et al. and Hovanessian et al.***

Claims 1-15 and 31-36 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Agrawal *et al.*, in view of Goodchild *et al.* and Hovanessian *et al.* Applicant respectfully traverses this rejection.

Claim 1 has been amended herein to incorporate the limitation of claim 2. However, Applicant respectfully submits that this amendment is not necessary to overcome the above rejection and has been made merely to facilitate prosecution.

Claim 2 has been cancelled herein; therefore, Applicant respectfully submits that the rejection with regard to claim 2 has been rendered moot.

The instant application claims a synthetic oligonucleotide having a nucleotide sequence specifically complementary to nucleotides 324 to 345 of a conserved *gag* region of the HIV-1 genome set forth as SEQ ID NO: 5, the oligonucleotide consisting of 21 nucleotides which are linked via phosphorothioate internucleotide linkages, wherein

the oligonucleotide comprises at least two 3′ terminal ribonucleotides, at least two 5′ terminal ribonucleotides, or at least two 3′-terminal and at least two 5′ terminal ribonucleotides. Also claimed are a method of treating HIV-1 or HIV-2 infection in a mammal comprising the step of administering to the mammal, such a synthetic oligonucleotide in an amount effective to inhibit the proliferation of HIV-1 or HIV-2, pharmaceutical formulations, methods of inhibiting HIV-1 or HIV-2 infection in a cell, and methods for introducing an intact oligonucleotide of the application into a mammal, whereby the oligonucleotide is present in intact form in the systemic plasma following oral administration.

The Office Action states at pages 11-12 that it would have been obvious to one of ordinary skill in the art to utilize antisense oligonucleotides of 21 nucleobases in length, and which sequences (*i.e.* of SEQ ID Nos: 1-4 of the instant invention) are embedded within the previously disclosed SEQ ID NO:1 of U.S. Patent No. 5,591,721, to target the gag HIV-1 gene *in vitro* in order to inhibit HIV infection *in vitro*, including HIV-1 and HIV-2 infections, because this larger antisense oligonucleotide of 25 nucleobases had been disclosed previously by Agrawal *et al.* for targeting the *gag* gene in order to inhibit HIV infections *in vitro*, and that it would have been obvious to utilize smaller sequences within this larger 25 nucleobase sequence. The Office Action further states at page 12 that one of ordinary skill in the art would have expected that the *in vitro* inhibition of *gag* expression by antisense, including the instantly claimed antisense of lengths of 21 nucleobases would lead to the *in vitro* inhibition of HIV-1 and HIV-2 replication *in vitro*, because the success of antisense inhibition of HIV *in vitro* had been demonstrated previously by Goodchild *et al.* and the similarities between HIV-1 and HIV-2 nucleic acids encoding the various viral proteins had been taught previously by Hovanessian *et al.* Applicant respectfully disagrees.

One of skill in the art would not have been motivated to use the claimed oligonucleotide complementary specifically to nucleotides 324 to 345 of a conserved *gag* region of the HIV-1 genome set forth as SEQ ID NO: 5 consisting of 21 nucleotides

which are linked via phosphorothioate internucleotide linkages, wherein the oligonucleotide comprises at least two 3′ terminal ribonucleotides, at least two 5′ terminal ribonucleotides, or at least two 3′-terminal and at least two 5′ terminal ribonucleotides, as claimed in the instant application. The specification of the instant application indicates at page 11, line 24 to page 12, line 11, that

> Novel antisense oligonucleotides have been designed which inhibit HIV-1 and HIV-2 replication. These olignoucleotides are synthetic oligonucleotides having phosphorothioate internucleotide linkages and a nucleotide sequence that is complementary to a portion of the *gag* region of the genome of HIV-1 and HIV-2. Sequences situated in this region have been demonstrated to be essential for viral packaging. . . . The oligonucleotides of the invention have been designed to bind to this region of RNA and DNA, thereby disrupting its natural stability and resulting ultimately in the inhibition of viral packaging and translation of *gag* mRNA. The specific sequence to which the oligonucleotides of the invention are complementary is nucleotides 324-345 of the *gag* region of HIV-1. This sequence is very conserved among strains of HIV-1, as shown below in TABLE 1.

This choice of these specific 21 nucleotide sequences was made for a specific purpose not suggested by the '721 patent. Furthermore, the '721 patent does not even indicate that the SEQ ID NO: 1 disclosed therein is complementary to an HIV sequence such as the *gag* sequence. Therefore, one of skill in the art would not have been motivated to specifically use the oligonucleotides claimed in the instant application.

Furthermore, one of skill in the art would not be motivated to combine the primary reference (the '721 patent) with Goodchild *et al.* or Hovanessian *et al.* to achieve the claimed invention.

Goodchild *et al.* refers to the use of the initiator codon for the *gag* gene as a possible sequence to which an oligonucleotide could be complementary, but does not refer to the nucleotides 324 to 345 of the *gag* gene, itself, and does not suggest using the *gag* gene, itself, as such a sequence.

Hovanessian *et al.* relates to transmembrane envelope proteins of HIV-2. Hovanessian *et al.* does not teach or suggest antisense oligonucleotides. Furthermore, Applicant submits that this reference teaches away from the expectation that the *in vitro* inhibition of *gag* expression by antisense would lead to the *in vitro* inhibition of HIV-1 and HIV-2 replication *in vitro*, by emphasizing the differences between HIV-1 and HIV-2, rather than their similarities. For example, this patent states that HIV-2 and SIV-mac share about 75% overall nucleotide sequence homology, but both of them are only distantly related to HIV-1 with about 40% overall homology (col. 1, lines 31-34).

Therefore, one of skill in the art would not be motivated to combine these references with the '721 patent. Accordingly, Applicant respectfully requests that the obviousness rejection of claims 1-15 and 31-36 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

CONCLUSIONS

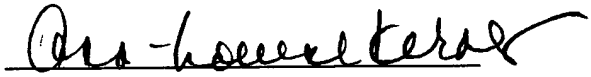
In view of the arguments set forth above, Applicant respectfully requests reconsideration and reexamination of the above-referenced patent application. Applicant submits that the rejections contained in the Office Action mailed on August 28, 2002, have been overcome, and that the claims are in condition for allowance.

Applicant encloses herewith a Petition for a Two Month Extension of Time pursuant to 37 C.F.R. § 1.136, until January 28, 2003, to respond to the Examiner's Office Action mailed on August 28, 2002. Please charge our Deposit Account No. 08-0219 the $205.00 fee for this purpose.

No other fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

If the Examiner believes that any further discussion of this communication would be helpful, please contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Attachments:
1.) Marked Up Version of Replacement Paragraphs in Specification
2.) Clean Copy of Pending Claims
3.) Compare Copy of Claims
4.) Galderisi *et al.*, J. Cell. Physiol. (1999) 181:251-57
5.) Agrawal, Antisense Therapeutics, (Sudhir Agrawal, ed.) 1996; p.v-vii
6.) Zamecnik, Antisense Therapeutics, (Sudhir Agrawal, ed.) 1996; p. 1-11
7.) Craig, *et al.*, Exp. Opin. Ther. Patents (1997) 7:1175-1182

Attachment 1
Marked Up Version of Replacement Paragraphs in Specification
U.S.S.N. 09/837,806
Filed April 18, 2001

Paragraph at page 4, line 24:

Thus, there still remains a need for a more effective anti-HIV oligonucleotide having therapeutic effects that are accompanied **by** fewer side effects, e.g., little cellular toxicity and reduced immunostimmulatory response.

Paragraph at page 7, line 24:

In yet another aspect, the invention provides pharmaceutical formulations suitable for inhibiting and treating HIV-1 or HIV-2 infection and having reduced side effects such as immunogenicity. These formulations ~~and for inhibiting comprising~~**comprise** at least one oligonucleotide in accordance with the invention in a pharmaceutically acceptable carrier.

Paragraph at page 7, line 33:

As used herein, a "pharmaceutically or physiologically acceptable carrier" includes any and all solvents (including but **not** limited to lactose), dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions of the invention is contemplated. Supplementary active ingredients can also be incorporated into the compositions.

Paragraph at page 8, line 14:

In another aspect, the invention provides a method of treating HIV-1 or HIV-2 infection in a mammal. In this method an oligonucleotide according to the invention is administered to the mammal in an amount effective to inhibit the proliferation of the virus. For purposes of the invention, the term "mammal" is meant to encompass primates and humans. In some embodiments, the oligonucleotide is orally administered to the mammal. The term "orally administered" refers to the provision of the formulation via the mouth through ingestion, or via some other part of the gastrointestinal system including the esophagus. In other embodiments, the oligonucleotide is administered via intravenous injection. In yet other embodiments, the oligonucleotide is administered colorectally. The term "colorectal administration" or "rectal administration" or "colorectally administered" refers to the provision of the pharmaceutical formulation of the invention to any part of the large intestine via surgical implantation, anal administration, or any other mode of placement therein.

Paragraph at page 11, line 3:

The patent and scientific literature referred to herein establishes the knowledge that is available to those with skill in the art. The issued U.S. patents, allowed patent applications, and articles cited herein are hereby incorporated by reference.

Paragraph at page 20, line 1:

The oligonucleotides described herein are administered to the mammal in the form of therapeutic pharmaceutical formulations that are effective for treating virus infection. These pharmaceutical formulations may be administered in conjunction with other therapeutic agents, e.g., AZT and/or various protease inhibitors, to treat AIDS.

Paragraph at page 24, line 10:

Administration of pharmaceutical compositions in accordance with **the** invention or to practice the method of the present invention can be carried out in a variety of

conventional ways, such as by oral ingestion, enteral, colorectal, or transdermal administration, inhalation, sublingual administration, or cutaneous, subcutaneous, intramuscular, intraocular, intraperitoneal, or intravenous injection, or any other route of administration known in the art for administrating therapeutic agents.

Paragraph at page 25, line 22:

When a therapeutically effective amount of composition of the invention is administered by injection, the synthetic oligonucleotide will preferably be in the form of a pyrogen-free, parenterally-acceptable, aqueous solution. The preparation of such parenterally-acceptable solutions, having due regard to ~~ph~~**pH**, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for injection should contain, in addition to the synthetic oligonucleotide, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. The pharmaceutical formulation can be administered in bolus, continuous, or intermittent dosages, or in a combination of continuous and intermittent dosages, as determined by the physician and the degree and/or stage of illness of the patient. The duration of therapy using the pharmaceutical composition of the present invention will vary, depending on the unique characteristics of the oligonucleotide and the particular therapeutic effect to be achieved, the limitations inherent in the art of preparing such a therapeutic formulation for the treatment of humans, the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Paragraph at page 26, line 26:

To determine the preclinical range of anti-HIV activity of various oligonucleotides of the invention (see TABLE 2), evaluations were performed with Oligo 12 (having SEQ ID NO:1), Oligo 32 (SEQ ID NO:3) and Oligo 41 (SEQ ID NO:6). These evaluations were performed to determine the activity of these compounds against a variety of wild type and drug-resistant strains of HIV-1, including both laboratory derived and low passage, clinical strains of virus and T-lymphocyte-tropic and monocyte-macrophage-tropic viruses ~~same~~**such** as ~~these are~~**those** listed below in TABLE 3.

Page 27, line 26

SI ~~-syncytiuminducing-~~ **syncytium inducing**

Paragraph at page 30, line 30:

In another set of experiments, the bioavailability of Oligo 12 was examined *in vivo* **and** was found to be intravenously and orally bioavailable to rats and monkeys after a single dose.